Compartment Calculation using the 'wnl' Package

Kyun-Seop Bae

2019-05-10

Contents

Introduction

We will show how to calculate drug concentrations using one- to three-compartmen model rapidly. Here is an example.

Dosing History

Dosing history is the following. At time 0 hour, 100 mg of a drug was administered by intravenous bolus. At time 24 hour, 150 mg of a drug was infused intravenously with the rate of 50mg/hr. At time 48 hour, 100 mg of a drug was administered orally.

Observation Time Points

With a given pharmacokinetic parameters, we would like to calculate the concentrations of a drug at the time of 0, 1, 2, 4, 8, 12 hour after each dosing.

Exercise 1. One-compartment model

If the drug is disposed by a one-compartment model with the pharmacokinetic parameters of Ka=1, Ke=0.1, F=1, and V=1, what would be the concentrations at the observation points?

Exercise 2. Two-compartment model

If the drug is disposed by a two-compartment model with the pharmacokinetic parameters of Ka=1, Ke=K10=0.1, K12=3, K21=1, F=1, and V=1, what would be the concentrations at the observation points?

Exercise 3. Three-compartment model

If the drug is disposed by a three-compartment model with the pharmacokinetic parameters of Ka=1, Ke=K10=0.1, K12=3, K21=1, K13=2, K31=0.5, F=1, and V=1, what would be the concentrations at the observation points?

Install 'wnl' Package

```
install.packages("wnl")
```

or for the latest version

```
install.packages("wnl", repos="http://r.acr.kr")
```

Load 'wnl' Package

```
require(wnl)
```

Data Preparation

```
DAT
```

```
##    TIME AMT RATE CMT DV
## 1     0 100    0   2 NA
## 2     1  NA   NA  NA NA
## 3     2  NA   NA  NA NA
## 4     4  NA   NA  NA NA
## 5     8  NA   NA  NA NA
## 6    12  NA   NA  NA NA
## 7    24 150   50   2 NA
## 8    25  NA   NA  NA NA
## 9    26  NA   NA  NA NA
## 10   28  NA   NA  NA NA
## 11   32  NA   NA  NA NA
## 12   36  NA   NA  NA NA
## 13   48 100    0   1 NA
## 14   49  NA   NA  NA NA
## 15   50  NA   NA  NA NA
## 16   52  NA   NA  NA NA
## 17   56  NA   NA  NA NA
## 18   60  NA   NA  NA NA
```

```
DAT2 = ExpandDH(DAT) ; DAT2
```

```
##    TIME AMT RATE CMT DV BOLUS RATE2
## 1     0 100    0   2  0   100     0
## 2     1   0    0   0  0     0     0
## 3     2   0    0   0  0     0     0
## 4     4   0    0   0  0     0     0
## 5     8   0    0   0  0     0     0
## 6    12   0    0   0  0     0     0
## 7    24 150   50   2  0     0    50
## 8    25   0    0   2  0     0    50
## 9    26   0    0   2  0     0    50
## 19   27   0    0   0  0     0     0
## 10   28   0    0   0  0     0     0
## 11   32   0    0   0  0     0     0
## 12   36   0    0   0  0     0     0
## 13   48 100    0   1  0   100     0
## 14   49   0    0   0  0     0     0
## 15   50   0    0   0  0     0     0
## 16   52   0    0   0  0     0     0
## 17   56   0    0   0  0     0     0
## 18   60   0    0   0  0     0     0
```

Note that time point 27 is added by **ExpandDH** function because it is a non-differentiable point.

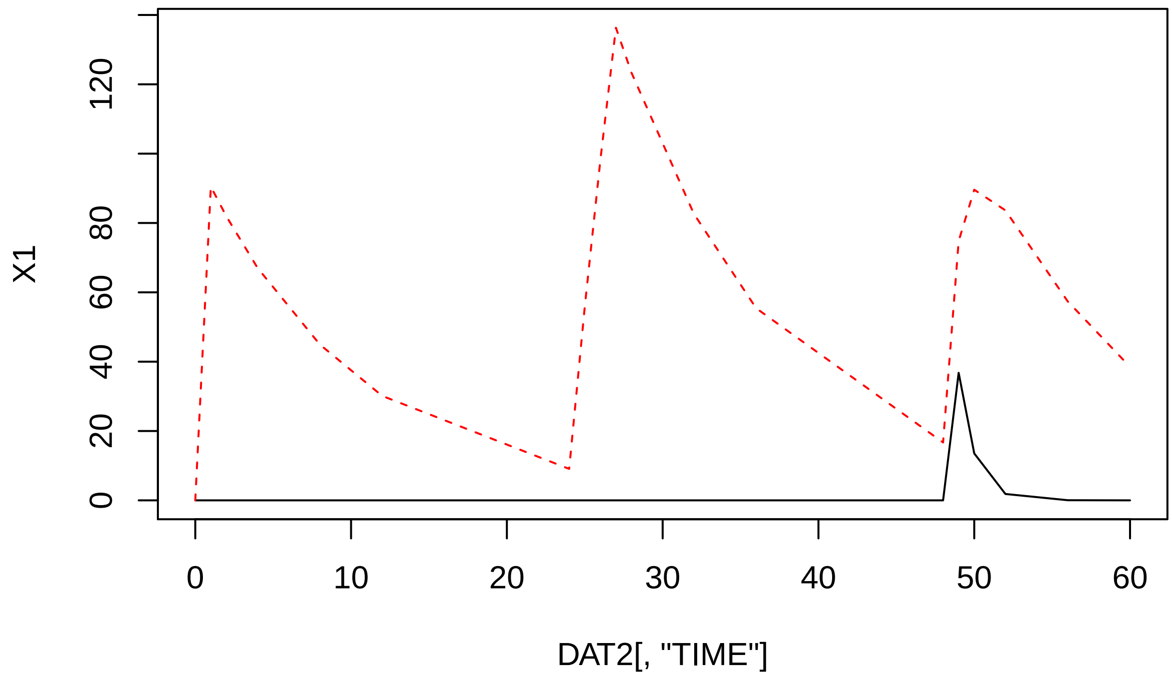
Solution 1

```
X1 = Comp1(Ke=0.1, Ka=1, DAT2) ; X1
```

```
##               [,1]       [,2]
##  [1,] 0.000000e+00   0.000000
##  [2,] 0.000000e+00  90.483742
##  [3,] 0.000000e+00  81.873075
##  [4,] 0.000000e+00  67.032005
##  [5,] 0.000000e+00  44.932896
##  [6,] 0.000000e+00  30.119421
##  [7,] 0.000000e+00   9.071795
##  [8,] 0.000000e+00  55.789791
##  [9,] 0.000000e+00  98.061981
## [10,] 0.000000e+00 136.311441
## [11,] 0.000000e+00 123.339692
## [12,] 0.000000e+00  82.677068
## [13,] 0.000000e+00  55.420096
## [14,] 0.000000e+00  16.692212
## [15,] 3.678794e+01  74.765736
## [16,] 1.353353e+01  89.599257
## [17,] 1.831564e+00  83.634059
## [18,] 3.354626e-02  57.388461
## [19,] 6.144212e-04  38.492939
```

Note that the first column is the depot(gut) compartment.

```
matplot(DAT2[, "TIME"], X1, type="l")
```



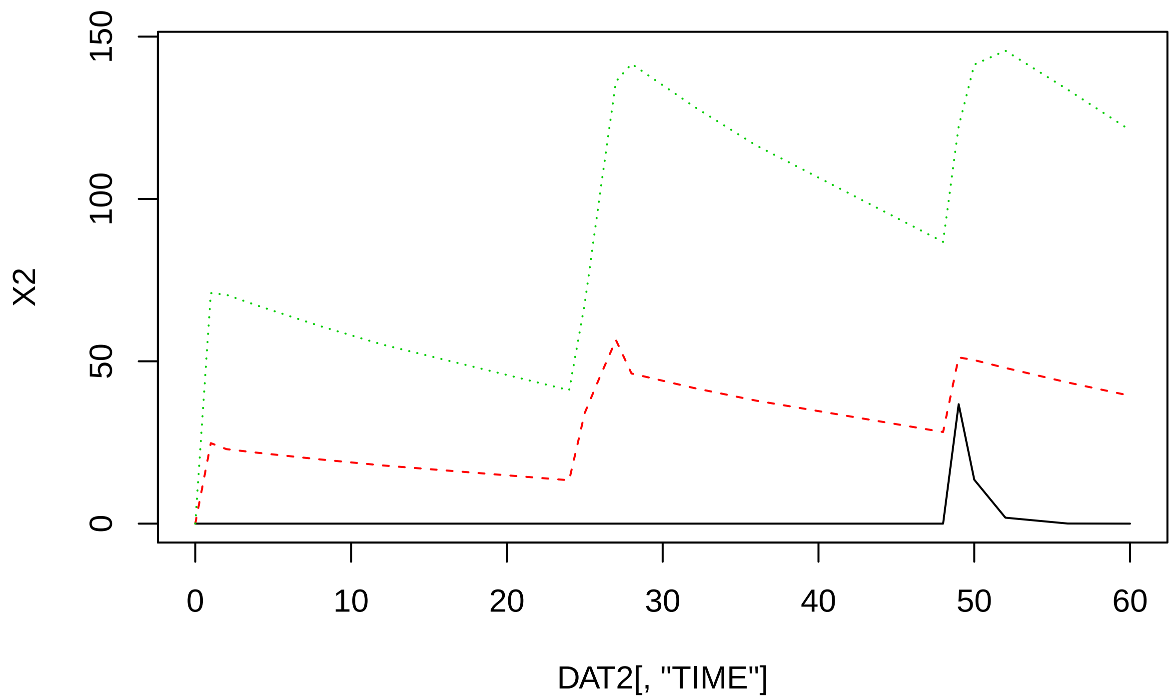
Solution 2

```
Sol = SolComp2(K10=0.1, K12=3, K21=1)
X2 = nComp(Sol, Ka=1, DAT2) ; X2
```

```
##                 [,1]     [,2]      [,3]
##  [1,] 0.000000e+00  0.00000   0.00000
##  [2,] 0.000000e+00 24.78579  71.00430
##  [3,] 0.000000e+00 22.94872  70.48922
##  [4,] 0.000000e+00 21.82887  67.13386
##  [5,] 0.000000e+00 19.78818  60.85782
##  [6,] 0.000000e+00 17.93827  55.16849
##  [7,] 0.000000e+00 13.36302  41.09748
##  [8,] 0.000000e+00 34.08869  67.74790
##  [9,] 0.000000e+00 45.53336 102.31559
## [10,] 0.000000e+00 56.55153 136.19086
## [11,] 0.000000e+00 46.25053 141.60095
## [12,] 0.000000e+00 41.78336 128.50319
## [13,] 0.000000e+00 37.87722 116.48999
## [14,] 0.000000e+00 28.21644  86.77862
## [15,] 3.678794e+01 51.20062 122.37609
## [16,] 1.353353e+01 50.36158 141.38048
## [17,] 1.831564e+00 47.95656 145.65708
## [18,] 3.354626e-02 43.47332 133.66703
## [19,] 6.144212e-04 39.40919 121.20089
```

The first column is the depot(gut) compartment. The second column is the central compartment and the third is the peripheral compartment.

```
matplot(DAT2[, "TIME"], X2, type="l")
```



Solution 3

```
Sol = SolComp3(K10=0.1, K12=3, K21=1, K13=2, K31=0.5)
X3 = nComp(Sol, Ka=1, DAT2) ; X3
```

```
##                [,1]      [,2]     [,3]      [,4]
##  [1,] 0.000000e+00  0.000000  0.00000   0.00000
##  [2,] 0.000000e+00 13.004819 44.19187  40.02386
##  [3,] 0.000000e+00 12.205766 39.85761  43.90691
##  [4,] 0.000000e+00 11.604779 35.94874  46.04289
##  [5,] 0.000000e+00 10.954285 33.31609  44.82325
##  [6,] 0.000000e+00 10.422939 31.66063  42.73598
##  [7,] 0.000000e+00  8.993606 27.31648  36.88080
##  [8,] 0.000000e+00 22.781008 46.57865  51.99548
##  [9,] 0.000000e+00 28.923842 67.17024  72.67283
## [10,] 0.000000e+00 34.824944 86.10027  94.65280
## [11,] 0.000000e+00 26.682954 84.48999 101.57568
## [12,] 0.000000e+00 24.912956 75.89143 101.67155
## [13,] 0.000000e+00 23.688228 71.96288  97.10912
## [14,] 0.000000e+00 20.438779 62.07916  83.81492
## [15,] 3.678794e+01 34.919791 87.37083 103.91654
```

```
## [16,] 1.353353e+01 33.228471 96.38124 116.45056
## [17,] 1.831564e+00 31.441383 95.92774 123.94904
## [18,] 3.354626e-02 29.630545 90.10716 121.19273
## [19,] 6.144212e-04 28.190201 85.63118 115.58182
```

The first column is depot(gut) compartment, and the following compartments are the central, the first peripheral, and the second peripheral compartment in order.

```
matplot(DAT2[, "TIME"], X3, type="l")
```